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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,775	11/23/2005	Ellen M. Welch	10589-044-999	7049

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EXAMINER	
VOGEL, NANCY TREPTOW	
ART UNIT	PAPER NUMBER
1636	
MAIL DATE	DELIVERY MODE
06/10/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,775	WELCH ET AL.	
	Examiner	Art Unit	
	NANCY VOGEL	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-45 and 47-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,30,33,37-51 and 1624* is/are rejected.

7)☒ Claim(s) *25,26,28,29,31,32,34 and 35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/15/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 16-35, 37-51 are pending in the case.

Receipt of the Information Disclosure Statement on 9/15/09 is acknowledged.

The following are new rejections:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16, 19 , 37-39, 41, 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rana (US Patent 6,503,721) in view of Gorski et al. (J. Mol. Evol., 1987, 24:236-251).

Rana discloses a method of identifying a small molecule that binds to a region of rRNA comprising contacting a rRNA with a library of small molecules under conditions that permit direct binding and formation of a complex and detecting the formation of the complex (see abstract, see col. 7-8). Regarding claim 19, the reference discloses that the rRNA may be labeled (see abstract). Regarding claim 37, the regions recited are present in the rRNA. Regarding claim 38, 39 the reference discloses that the small molecules may be attached to a solid support (abstract) which may be beads, plastic, polystyrene, etc. (see col. 16). Regarding claim 41, the rRNA is labeled with phosphorescent, fluorescent, ultraviolet, infrared, visible dyes (col. 13). Regarding claim 44, the reference discloses that the complex is detected by such techniques as fluorescence spectroscopy (see col. 21). Regarding claim 45, 46 the structure of the small molecule can be determined, by such methods as NMR (see col. 17, 18). The difference the reference and the instant claims is that the human 28S rRNA is recited. However, human 28s rRNA is disclosed by Gorski et al. (J. Mol. Evol., (1987) 24:236-251). It would have been obvious to have used the method disclosed by Rana, applied to the human 28srRNA, disclosed by Gorski et al., since Rana disclose that the method may be used for identifying compounds in a library which bind or interact with any ribosomal RNA, and since human 28s rRNA is known in the art as disclosed by Rana. One would have been motivated to have used 28s rRNA since the human 28s rRNA is known to be important in protein synthesis in human cells and since the identification of compounds which bind to said human 28s rRNA would be useful.

Claims 16-24, 38, 39, 41-44, 47-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beckmann et al. (WO 01/44516) in view of Rana (US Patent 6,503,713) and Gorski .et al. (J. Mol. Evol., (1987) 24:236-251)

Beckmann et al. disclose a method of identifying a molecule that modulates premature translation termination or nonsense-mediated mRNA decay comprising contacting the molecule with a cell containing a nucleic acid sequence comprising a regulatory element operably linked to a reporter gene, wherein the reporter gene comprises a premature stop codon, and detecting the protein expressed from the reporter gene wherein a molecule that modulates premature translation termination or non-sense-mediated mRNA decay is identified if the protein expressed from the reporter gene in the presence of the molecule is altered relative to the protein expressed from the reporter gene in the absence of the small molecule or the presence of a negative control (pages 2 line 19 – page 3 line 5) (17). The molecule may be a small chemical molecule (page 8 lines 25-31, page 19 lines 1-page 20 lines 25). The molecule can be may comprise benzodiazepines, isoprenoids, thiazolidinones, metathiazonones, morpholinos, (page 20, lines 1-20) (claim 43). The cell can be a hybridomas, a pre-B, a 293, a HeLa, a HepG2, a K562, or a 3T3 cell (page 7 lines 27-34) (claim 21). The reference teaches that an in vitro translation cellular extract may be used instead of a cell (see page 2, lines 19-25) (18). The reference discloses that the cellular extract may be rabbit reticulocyte, (23), HeLa (22-24). The molecule of interest can be bound to a solid state component, such as a glass surfaces (page 22) (claim 38, 39). A label can be used for a component of the assay, such as fluorescent dyes, radiolabels, enzymes,

spectroscopic colorimetric label (see page 23) (claim 19, 20, 41, 42,). Detection may be by spectrophotomery, scintillation, etc. (claims 44). The reference discloses that the premature stop codon is UAA, UAG, or UGA, and UAA may be present (see Fig. 1) (claim 47). Since the claims recite UAAG, UAAA, UAAC, and UAAU as embodiments, and the reference discloses the UAA premature stop codon, the reference discloses at least one of the above 4 nucleotide embodiment. An increase in protein expressed in the presence of the molecule relative to the amount of protein expressed in its absence would indicate that the molecule suppresses premature translation termination or nonsense-mediated mRNA decay, and conversely, a decrease would indicate the ;molecule enhances premature translation termination or nonsense-mediated mRNA (claims 50, 51).

The difference between the reference and the instant claims is that a first step of contacting a target RNA which is a human 28S rRNA or a "region" of human 28S rRNA with a library of small molecules under conditions that permit direct binding of the target RNA to a member of the library, and detecting the formation of a target RNA: small molecule complex, wherein a small molecule that binds to the target RNA is identified if a target RNA:small molecule complex is detected, is included.

However, Rana (US Patent 6,503,721) discloses a method of identifying a small molecule that binds to a target RNA comprising contacting a target RNA, which may be any RNA, including any ribosomal RNA, with a library of small molecules, and detecting whether a complex is formed between the RNA and a small molecule (see col. 6-7). Gorski et al. disclose human 28S rRNA. It would have been obvious to one of ordinary

skill in the art to have included such steps as disclosed by Rana, using the human 28S rRNA of Gorski, or any rRNA which contains any two nucleotides contained in the human 28S rRNA (i.e. a region of human 28S rRNA) in the method of Beckmann, as a preliminary screen to identify possible candidates for molecules that modulate premature translation termination or nonsense-mediated mRNA decay, since Rana and Beckmann are each concerned with isolating molecules which may interfere with binding a proteins to RNA, or more generally, with isolating molecules that bind to an RNA of interest. One would have been motivated to do so by the teaching of Rana that any RNA of interest may be tested for binding to compounds in library of binding candidates, and particularly any ribosomal RNA, for the purpose of the identification of compounds or molecules that may be useful in such areas as treatment of diseases or generally gene regulation (see abstract), and by the teaching of the human 28S rRNA by Gorski. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 27, 30, 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beckmann et al. (WO 01/44516) in view of Rana (US Patent 6,503,713) and Gorski (J. Mol. Evol., (1987) 24:236-251) as applied to claims 16-24, 38, 39, 41-44, 47- 51 above, and further in view of Shiroki et al. (In Vitro Translation Extracts from Tissue Culture Cells, Methods in Molecular Biology, 118, pages 449-458, 1999).

Beckmann et al. and Rana and Gorski are cited essentially for the reasons set forth above. The difference between the reference and the instant claims is that particular cell free extracts are used.

However, Shiroki et al. discloses S10 extracts from HeLa cells used for in vitro translation. It would have been obvious to have used any particular known cell extract known to be useful for in vitro translation, since such extracts were well known in the art as evidenced by Shiroki et al., and since the use of any particular extract for its known and useful properties would have been obvious to one of ordinary skill in the art. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beckmann et al. (WO 01/44516) in view of Rana (US Patent 6,503,713) and Gorski (J. Mol. Evol., (1987) 24:236-251) as applied to claims 16-24, 38, 39, 41-44, 47- 51 above, and further in view of Yang et al. (US Patent 7354709).

Beckmann et al. and Rana and Gorski et al. are cited essentially for the reasons set forth above.

The difference between the claim and the references is that the small molecule library is present on a chip.

However, Yang et al. teach that chips containing small libraries of such compounds as pyrrolinines, isoprenoids, benzodiazapines, thiazolidinones, metathiazoanones are known in the art (see col. 13 line 50 – col. 14, line 25). It would

have been obvious to utilize chips containing libraries of chemical molecules since such chips were well known in the art as evidenced by Yang et al., and since the advantages of using chip technology which include such known benefits of miniaturization and ease of analysis were well known to be obtained using chips and computer technology. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 45 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beckmann et al. (WO 01/44516) in view of Rana (US Patent 6,503,713) and Gorski J. Mol. Evol., (1987) 24:236-251 as applied to claims 16-24, 38, 39, 41-44, 47-51 above, and further in view Berger et al. (US 2004/0162345)

Beckmann and Rana and Gorski are cited essentially for the reasons set forth above.

The difference between the claims and the references is that the method further comprises determining the structure of the compound, by mass spectroscopy, NMR, X-ray crystallography, Edman degradation or vibration spectroscopy.
However, as evidenced by at least Berger et al., determining the structure of a candidate compound following its identification as useful was well known at the time of the invention. Berger disclose for example that compounds of a chemical library that are candidate compounds may be analyzed in their structure by such well known techniques as mass spectroscopy or NMR (para. 0161). Therefore, absent an

unexpected result it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to modify them method of Beckmann et al. in view of Rana wherein a compound identified by the assays disclosed is further analyzed to determine its structure. The motivation to make the modification recited above arises from the desire to understand the mechanism of the compound's activity thereby providing a starting point to identify other structurally similar compounds with improved properties over the lead compound. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 25, 26, 28, 29, 31, 32, 34, 35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

NV
6/2/10